UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/635,974	08/09/2000	Thomas Teufel	381-86	5643

7590 05/12/2006

Deborah A. Somerville
Kenyon & Kenyon
One Broadway
New York, NY 10004

EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 05/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/635,974	TEUFEL, THOMAS	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The arguments filed on March 21st, 2006 is acknowledged.

2. Claims 2, 6-45 have been cancelled.

Claims 1, 3-5 and 46-48 are pending and examined on the merits.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Response to Arguments

4. The rejection of claims 1, 3-5 and 46-48 under 35 USC 112, first paragraph is maintained.

The response filed on March 21st, 2006 has been carefully considered but is deemed not to be persuasive. The response states that "rejection is improper because the Examiner has not met the initial burden of establishing a reasonable basis for questioning what is provided by the specification..... the specification discloses treatment of a hypeproliferative disease (ag., psoriasis) by sole administration of an EGFR antibody or other EGFR antagonist (e.g.,page 3, lines 9-15.....The Examiner argues that a claim directed to treatment of psoriasis with an EGFR antibody is not commensurate with the scope of the specification because the working example describes a treatment in which CPT-11 is co-administered.....Although the Examiner presupposes that CPT-11 is somehow required for the observed improvement in psoriasis, there is no such suggestion in the specification. The Applicant further argues that "The Examiner's position appears to tum on the supposition that CPT-11must be

administered in order for there to be a response. However, while the Examiner has deemed the Applicant's arguments to be unpersuasive, the Patent Office still has not met its burden of providing a reasonable basis for its position that the pending claims are not enabled. Nor has the Examiner provided any rationale for the belief that administration of CPT-11 would have any use for treatment of psoriasis. To establish a reasonable basis, the Examiner must provide a reasonable explanation as to why the scope of protection of a claim is not adequately enabled by the disclosure...The unpredictability presumed by the Examiner springs from an unsupported supposition that CPT-11 is essential for the psoriasis resolution that is observed in the working example. In summary, the Applicant asserts that the scope of the pending claims is reasonably enabled by the specification and that no undue experimentation is necessary to practice the claimed invention".

The response filed has been carefully considered but is deemed not to be persuasive. As stated in the previous office action a mere contemplation of the treatment of the hyperproliferative disease with an EGFR antibody or other EGFR antagonist, and the data presented in the examples of the instant application does not convince one skilled in the art that the applicant is enabled for the scope of the invention as claimed. As stated by the examiner in the office action mailed on 01/03/2005, the specification confines its teachings to methods comprising the administration to a cancer patient, who happened to also suffer form psoriasis, of a specific of a specific

chimeric version of the murine 225 antibody anti-EGFR antibody in combination with a chemotherapeutic agent with is designated at "CPT-11(cisplatin)"

Because the specification teaches that a human cancer patient was administered in combination of the antibody C225 and a chemotherapeutic agent that was wither CPT-11 or cisplatin, it is not clear whether the psoriasis was improved because of the C225 administration, the chemotherapeutic agent (CPT-11 or cisplatin) administration, of the combination of two. In contrast to the working examples provided by the specification and the argument presented by the applicant "the applicant discovered that the improvement in psoriasis was .....use the anti-EGFR/HER1 antibody alone (pages 5-6 of the response)", the scope of claims is broadly drawn to the treatment of psoriasis with an EGFR antibody and does not commensurate in scope of what the applicant is discussing. And further because the specification teaches that a human cancer patient was administered in combination of the antibody C225 and a chemotherapeutic agent that was wither CPT-11 or cisplatin, it is not clear whether the psoriasis was improved because of the C225 administration, the chemotherapeutic agent (CPT-11 or cisplatin) administration, of the combination of two. In contrast to the working examples provided by the specification and the argument presented by the applicant "the applicant discovered that the improvement in psoriasis was .....use the anti-EGFR/HER1 antibody alone (pages 5-6 of the response)", the scope of claims is broadly drawn to the treatment of psoriasis with an EGFR antibody and does not commensurate in scope of what the applicant is discussing.

Disclosure of treatment of a human with psoriasis, comprising systemically administering to said human an amount of an EGFR/HER1 antibody in combination with a chemotherapeutic agent is insufficient support for claims which are broadly drawn to a method of treating psoriasis using the antibody alone. The applicant states that "even though the examples describe co administration of an anti-EGFR/HER1 antibody with a therapeutic agent, the specification clearly sets forth how to use the anti-EGFR/HER1 antibody alone" (page 5 last paragraph). This argument is deemed not to be persuasive because it is the applicants' responsibility to provide the office with enough evidence to support and that is commensurate within the scope of the claimed invention.

Due to the nature of the art, it is hard to convince an ordinary skilled in the art that it is possible to treating a human with psoriasis comprising administering only EGFR/HER1 antibody, because the studies repeatedly show, for example Rockwell et al (U.S. patent 5,840,301; Date of Patent November 24th, 1998) that treatment with antibodies combined with an anti-chemotherapeutic agent such as doxorubicin, cisplatin or taxol provides a more efficient treatment for inhibiting the growth of tumor cells than the use of the antibody by itself (column 6 lines 15-40, in particular). Rockwell et al teach the combined treatment of one or more antibodies with an anti-neoplastic agent or an anti-chemotherapeutic agent, but not the treatment with antibody alone, provides an effective regimen for treatment.

Van de Winkel et al (PGPUB 20030194403; Publication Date October 16th, 2003) (paragraph 0282) teach that the human anti-EGFR antibodies, or antigen binding

fragments thereof, can be co-administered with a therapeutic agent, e.g., a chemotherapeutic agent, an immunosuppressive agent, an ant-inflammatory agent, or an anti-psoriasis agent and such therapeutic agents include, among others, anti-neoplastic agents such as cisplatin. Cisplatin is intravenously administered as a 100 mg/m.sup.2 dose once every four weeks and adriamycin is intravenously administered as a 60-75 mg/m.sup.2 dose once every 21 days. All the studies in Van de Winkel consist of the administration of anti-EGFR antibodies along with a therapeutic agent, but not anti-EGFR antibodies alone.

The studies showing an increase or an improvement in the treatment of cancers using antibody conjugates have been well published in the art. Antibody based drug targeting is also a very well known field with promising research underway. The prior art search reveals several cases wherein the antibody conjugates yield better results and better treatment regimen than the antibody alone. As such, since the specification reveals studies using anti-EGFR antibody and Cisplatin and not with anti-EGFR alone, the claims are still considered not commensurate in scope.

Further, Varani (cited in a previous Office action) teaches that an impediment to understanding the pathophysiology of psoriasis is the lack of good experimental models (see page 254, lst column) and that there are no animal models of psoriasis. Therefore, it is not clear that the results provided in the specification may be applicable to any mammal other than humans. Furthennore, the C225 antibody was administercd in combination with a second drug, making it unclear whether the results provided in the specification may be applicable to the treatment of psoriasis comprising administration

of an EGFR/HERI antibody in an amount effective to treat psoriasis, because the specification fails to teach an amount of an EGFR/HERI antibody effective to treat psoriasis. In view of the unclear teachings of the specitication conceming the identity of the second drug combined with the C225 antibody, the lack of controls demonstrating that the C225 antibody would be effective if used alone for the treatment of psoriasis, the lack of animal models, and the lack of teachings demonstrating how results demonstrating that C225 in combination with a second drug, the identity of which is unclear, would extrapolate to the broad scope of methods comprising the use of any anti-EGFR/HERI antibody, the practice of the claimed inventions would require further and undue experimentation on the part of the skilled worker. Therefore, the claimed inventions are not supported by the specification.

The specification fails to provide any additional guidance or working examples that other EGFR family members, other antagonists, or other disorders would be subject to the same treatment efficacy instantly exemplified. No mechanism of action is taught or suggested, and no guidance is provided as to rational design for antagonists of other EGFR ligand stimulated disorders.

Therefore in light of the breadth of the claims, the lack of guidance and working examples in the art, the unpredictable nature of the art of cancer treatment, one of skill in art would not be enabled to practice the full scope of the invention and the rejection is maintained.

5. The rejection of claim 48 under 35 USC 112, first paragraph is maintained.

The response filed on March 21st, 2006 has been carefully considered but is deemed not to be persuasive. The response states that C225 is a chimeric antibody with a murine variable region (heavy and light chain variable domains) and human constant region (heavy and light chain constant domains). The specification specifically refers to .... C225 is not a humanized antibody. ... the CDRS and frameworks are native .... the specification also provides that preferred çhimeric antibodies are derived from .... U.S. Patent No.4,943,533. Thus, the instant specification discloses all of the amino acid sequences that affect antibody confirmation and determine binding properties, and one of ordinary skill in the art can practice the invention of Claim 48. Applicant respectfully requests that the rejection be withdrawn.

In response to this argument, while the monoclonal antibody, 225, is publicly available, and the specification indicates that the chimerized 225 antibody can be synthesized from the methods provided in Wels et al (IDS – 12/27/2004), neither the reference provided nor the specification fails to describe how to make species of chimerized 225 antibody, C225 that is referred to in claim 48. The specification discloses that C225 is a chimerized version of Mab225 and C225 is otherwise known in the art. As stated in the previous office action, the specification fails to provide enough information for one of ordinary skill in the art to produce a chimeric antibody with exactly the same characteristics as the C225 antibody, because the specification fails to provide the structure and specific sequence for the claimed C225 antibody. The specification provides the complementary determining regions for the antibody 225 which are same for C225. However, it is well known in the art, that the amino acid

sequence of the framework regions and regions other than the CDR portion can affect the structural conformation of an antibody and determine its antigen binding properties. The applicant cannot refer to the previous literature or patent for the parent antibody and interpret that the chimerized version of the antibody or the sequence of the fully functional antibody is public knowledge. Thus, because it does not appear that the C225 antibody is publicly available, and because the specification does not provide the structure of the C225 chimeric antibody, one of ordinary skill in the art cannot be assured of the ability to practice the claimed invention that requires the use of the specific species of chimerized 225 antibody, C225.

Conclusion

6. No claims are allowed

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

8. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi, Ph.D.
Ph: (571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER